

Attorney Docket No.: CLON-008

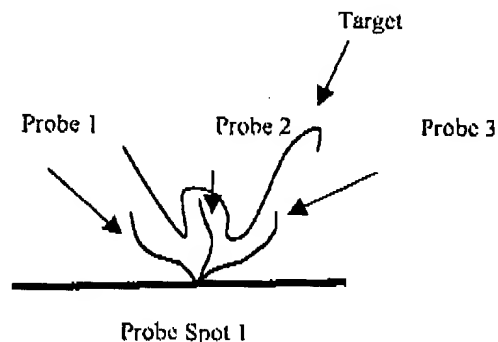
Clontech Ref: P-60

U.S. Serial No.: 09/417,268

indefinite. In view of the above amendments to the claims substituting "attached" for "stably associated therewith" pursuant to the Examiner's rejection, this rejection may be withdrawn.

In the Office Action, Claims 1-3, 5, 10, 12, 13, 57, 60-62, 64, 69 and 71-72 were rejected under 35 U.S.C. § 102 as being anticipated by Letsinger et al (U.S. Pat. No. 5,681,943).

As amended, each distinct probe oligonucleotide of each spot of the mixture that makes up each probe composition of the claimed arrays must be attached to the surface of the solid support of the array. As such, if the array is made up of a plurality of probe compositions, where each composition consists of two different oligonucleotide probes, each of the two different oligonucleotide probes is attached to the array. Likewise, if the array is made up of probe compositions where each composition consists of three different oligonucleotide probes, each of the three different oligonucleotide probes is attached to the array as illustrated below:



Turning now to Letsinger, Letsinger never teaches such an array structure as is required in the present claims. In Letsinger's suggested arrays, each probe spot is made up of only a single nucleic acid attached to a substrate surface. This single nucleic acid may be the target nucleic acid or one of the two probe nucleic acids. However, only a single nucleic acid is attached in each spot, not two or more different nucleic acids as is required in the claimed invention.

Attorney Docket No.: CLON-008

Clontech Ref: P-60

U.S. Serial No.: 09/417,268

In using Letsinger's suggested array, one produces a structure in each positive spot of the array that is made up of a long target nucleic acid hybridized to two distinct probe oligonucleotides that, upon hybridization to the target autoligate to each other. However, even in this post hybridization structure, only one of the probes is attached to the surface of the support, as illustrated in Figure 4 of Letsinger. Nowhere in Letsinger is there a teaching of an array where each spot includes two or more probes that are both attached to the solid support.

Accordingly, because Letsinger fails to teach an array as claimed where each spot includes two or more different oligo probes that are each attached to the surface, Letsinger fails to anticipate the claimed invention and the rejection of Claims 1-3, 5, 10, 12, 13, 57, 60-62, 64, 69 and 71-72 under 35 U.S.C. § 102 as being anticipated by Letsinger et al (U.S. Pat. No. 5,681,943) may be withdrawn.

Claims 4-10, 14-17, 58, 63, 65-68 and 73-76 have been rejected under 35 U.S.C. §103(a) over Letsinger in view of Pinkel. As demonstrated above, Letsinger is fundamentally deficient in failing to teach a structure where each probe composition includes two or more probe oligonucleotides that are each attached to the support surface. In addition, the Pinkel reference fails to make up this fundamental deficiency in Letsinger because Pinkel does not even teach that each probe spot contain at least two different oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex of the target nucleic acid and the at least two different oligonucleotide probes. Accordingly, this rejection may be withdrawn.

Claims 53, 59 and 77 were rejected under 35 U.S.C. §103(a) over Letsinger in view of Stratagene. As demonstrated above, Letsinger is fundamentally deficient in failing to teach the structure of the claimed arrays where the two or more probes of each spot are attached to a solid support. As Stratagene has been cited solely for motivation to make a kit, this reference fails to make up the fundamental deficiency in Letsinger. Accordingly, the

Attorney Docket No.: CLON-008

Clontech Ref: P-60

U.S. Serial No.: 09/417,268

claimed invention is not obvious over the combined teaching of Letsinger in view of Stratagene and this rejection may be withdrawn.

Claims 11 and 70 were rejected under 35 U.S.C. §103(a) over Letsinger in view of Lockhart. As demonstrated above, Letsinger is fundamentally deficient in failing to teach the structure of the claimed arrays where the two or more probes of each spot are attached to a solid support. As Lockhart has been cited solely for the teaching of a mis-match probe element, this reference fails to make up the fundamental deficiency in Letsinger. Accordingly, the combined teaching of Letsinger in view of Lockhart does not make the claimed invention obvious and this rejection may be withdrawn.

In view of the attached amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) An array comprising at least one pattern of probe oligonucleotide spots ~~stably associated with the~~ attached to a surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence each attached to said surface of said solid support that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.
57. (Amended) An array comprising a pattern of probe oligonucleotide spots, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition consisting of a mixture of 3 to 50 unique oligonucleotides of different sequence and from about 15 to 150 nucleotides in length that are each attached to a surface of a solid support and hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.
58. (Amended) An array comprising a pattern of probe oligonucleotide spots of a density that does not exceed about 400 spots/cm<sup>2</sup>, wherein each probe oligonucleotide spot consists of a mixture of 3 to 20 unique oligonucleotides of different sequence and from about 25 to 100 nucleotides in length that are each attached to a surface of a solid support and hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.
60. (Amended) An array comprising at least one pattern of probe oligonucleotide spots ~~stably associated with the~~ attached to a surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that are each attached to said surface of said solid support and cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.